

OPHTHALMIA NEONATORUM

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In 1884 a collective survey conducted by the then recently established Ophthalmological Society of the United Kingdom showed that between 30 to 41 per cent. of inmates at blind schools and institutions had been blinded by ophthalmia neonatorum. As this survey included adults as well as children it is clear that considerably more than 30 per cent. of all blind children at that time had lost their sight through ophthalmia neonatorum. In 1922 the Ministry of Education in a survey at blind schools found that 28.5 per cent. of the children at such schools were blind from this affection. A parallel investigation carried out in 1944 showed a marked decline: ophthalmia neonatorum was now responsible for not more than 9.2 per cent. Between 1884 and 1922 there had therefore been some decline, possibly a considerable decline, in the incidence of blindness from ophthalmia neonatorum, but the decline registered between 1922 and 1944 is of considerable magnitude. It is likely that in the course of the present decade blindness from ophthalmia neonatorum will have become rare. One may assume this from the fact that in the seven years 1941-47 only five infants are known to have been blinded from ophthalmia neonatorum throughout the whole of England and Wales.

Factors in the Decline of Blindness from Ophthalmia Neonatorum

Three distinct developments are responsible for this gratifying decline.

(1) **Credé Technique.**—In the first place there must have been a considerable decline in the incidence of ophthalmia neonatorum from the widespread application of the Credé technique, which was developed in the '80s of the last century. How beneficial that practice was is brought out by Stephenson (1907).

(2) **Compulsory Notification and Facilities for Treatment.**—In spite of the wide acceptance of

Credé's teaching, ophthalmia neonatorum still continued to exact a drastic toll, and this led to a movement in which many ophthalmic surgeons and progressive local authorities were concerned. It was their aim to provide adequate facilities for treatment, and their pioneer work culminated in a Statutory Order promulgated in 1914, which made ophthalmia neonatorum a notifiable disease, and imposed upon the local authorities the obligation of either satisfying themselves that adequate treatment was available to the affected infant, or of providing such treatment. Though there is no adequate statistical evidence there is much to indicate that it was this statutory enactment which initiated the downward trend in the incidence of blindness from ophthalmia neonatorum. The decline was so steady that in the four years 1934-37 the number of babies reported as blind from ophthalmia neonatorum was 6, 7, 8, and 7 respectively for the whole of England and Wales. These figures must be reliable because the outcome of treatment under the order must be recorded. Blindness from ophthalmia neonatorum had therefore ceased to be a mass problem, and had become reduced to occasional tragedies. That ophthalmia neonatorum was, however, still a formidable affection is seen from the fact that in 1938 the number of blinded babies had increased to ten, whilst the number whose vision had been impaired by the infection was 30, 36, 36, 31, and 24 respectively for each of the five years 1934-38.

(3) **Newer Methods of Treatment.**—The almost total elimination of blindness and impaired vision from ophthalmia neonatorum obtaining today must be ascribed to the influence that began to exert itself by about 1940. The sulphonamides replaced the classical methods of treatment and reduced the duration of ophthalmia neonatorum from weeks to as many days, greatly eliminating the danger of corneal involvement.

The movement begun in the 1880s which aimed at prophylaxis, the activities of the early years of this century which aimed at adequate facilities for treatment, and the recent developments in chemotherapy and the antibiotics, have together achieved a result as striking as any in the annals of public health.

Compulsory Notification

The reduction in the incidence of ophthalmia neonatorum following the use of the Credé method of prophylaxis is now a matter of history. In England and Wales the focal point in the decline of blindness from ophthalmia neonatorum is undoubtedly the Statutory Order of 1914. Prior to 1914 some of the more progressive local authorities had made ophthalmia neonatorum notifiable and had provided facilities for treatment, and it was the very success of these experiments in notification that led to the general order. That order, rightly, made no distinction in the different aetiological types, or in the degree of severity of the affection. Ophthalmia neonatorum for the purpose of this order was defined as a 'purulent discharge from the eyes of an infant commencing within 21 days from the date of its birth'. It imposed on both midwives and medical attendants the duty of notifying the affection. The order was modified in 1936, when the duty of notification was laid exclusively on the medical attendant; the duty of a midwife was now to summon medical assistance in a case of 'any inflammation or discharge from the eyes, however slight'. This modification, whilst it imposes no extra obligation on the medical attendant, has ensured that no mild case under the care of a midwife is overlooked—an important development since a mild case may well become severe within a matter of hours. In contrast to the practice obtaining in many countries notification of ophthalmia neonatorum in England and Wales does not, therefore, mean notification of proved gonococcal cases: purulent conjunctivitis in the newborn from any cause is notifiable. It is likely that at the time when the order was promulgated it was generally assumed that most cases were gonococcal in origin. This is certainly not true today, and it is fortunate that the order was sufficiently elastic to cover all cases, for it is not only gonococcal ophthalmia which may lead to disastrous results; other organisms may be equally responsible.

In consequence of the order statistical data on the number of cases of ophthalmia neonatorum seen in England and Wales is now available from 1914 onwards. The rate per thousand has shown a slow decline between 1914 and 1948, but it would be fallacious to accept this as undoubted evidence of

a decline in the incidence of the affection. Since the purpose of the order was to ensure that early and adequate treatment was available rather than to provide statistics on ophthalmia neonatorum, the tendency has been to notify cases that are only doubtfully ophthalmia neonatorum. The success of the order must therefore be judged not by any decline in the number of infants notified, but by the decline recorded almost year by year in the incidence of impaired vision and blindness from the affection. By this criterion the order has been brilliantly successful. In itself the order was the most significant development in the conquest of blindness from ophthalmia neonatorum, and that was its supreme achievement. But it also served an immensely useful purpose in creating the incidental machinery whereby the newer methods of chemotherapeutic treatment, when they came some fifteen years ago, could be effectively exploited.

Bacteriology

The view generally held that ophthalmia neonatorum is synonymous with gonococcal ophthalmia is erroneous. Though there are differences in detail, most series of cases of ophthalmia neonatorum show that the affection is produced by a great variety of organisms, and in many series the gonococcus is not the predominant causal organism. It was responsible for about 25 per cent. of all cases in a series of 737 seen at the ophthalmia neonatorum unit at White Oak Hospital between 1939 and 1945. *Staphylococcus aureus* accounted for about 35 per cent. of cases, whilst the meningococcus, pneumococcus, streptococcus, and other coccal organisms each contributed a small percentage. Bacilli were responsible for about 20 per cent. of cases, diphtheroids being the commonest, but the Koch-Weeks bacillus was not a curiosity as a causal organism.

Recent series, like the older series, contain some 10 to 20 per cent. of cases in which no micro-organism can be found in the smear or culture. Most of these 'negative' cases do not represent faulty bacteriological examination, but are examples of ophthalmia neonatorum due to virus infection. This virus has not been isolated in culture, but its existence has been demonstrated by animal inoculation, and by the presence of inclusion bodies in the conjunctival epithelium—a finding responsible for the designation of inclusion ophthalmia neonatorum, or inclusion blenorrhoea. Inclusion blenorrhoea is part of a clear-cut venereal disease. In the mother of the affected baby a scraping of the epithelial cells taken from the transitional lining at the os generally also shows inclusion bodies. To complement ophthalmia neonatorum in the baby and inclusion cervicitis in the mother, there is the non-specific

urethritis in men, where inclusion bodies can also be demonstrated in epithelial scrapings. This virus infection appears to be fairly widespread in the community, it gives minimal clinical symptoms, and not infrequently it is sub-clinical.

Prophylaxis

The essential measure of prophylaxis in ophthalmia neonatorum is the treatment of maternal infection during pregnancy. In the light of present knowledge this means more than the treatment of active or chronic gonorrhoea, or even of leucorrhoea. Ophthalmia neonatorum will be eliminated only when maternal infections are eliminated.

The more immediate method of prophylaxis associated with the name of Credé is immensely valuable, but has distinct limitations. The mechanical part of the procedure—the cleansing of the lids as soon as the head is born and before the baby is allowed to open its eyes, and the care taken to prevent any contaminated bath water reaching the baby's eyes—is now part of the routine of delivery, and is consistent with the principles of asepsis. The chemical component of the procedure—the instillation of silver or some other disinfectant into the eye—is of doubtful value and is a relic of Listerian antisepsis. It is a moot point whether an infected conjunctival sac will be disinfected by the application of one drop of an antiseptic. There seems to be no reason for using silver nitrate, as this is far from being a foolproof agent. There is nothing to indicate that it is superior to the organic silver preparations, which at any rate are innocuous. If anything is to be put into the baby's eyes it is best to put in two or three drops of 20 per cent. argyrol, rather than 1 per cent. silver nitrate. There is nothing to be said for drops of sodium sulphacetamide ('albugid'); they are largely ineffective locally. And there is nothing to suggest that a drop of

penicillin will disinfect a presumably infected surface by momentary contact.

Treatment

The classical methods of treatment have no place in the treatment of ophthalmia neonatorum today. Those methods consisted essentially of ceaselessly washing away all the pus from the infected eye to prevent the pus from damaging the cornea, and waiting for spontaneous healing which generally took some weeks. Such adjuvants as were used—antiseptic drops and occasionally shock therapy by milk injections—probably had little effect on the infection. The classical methods of treatment, therefore, did little more than prevent complications. Their value against the infection itself was always problematical.

In contrast the modern methods of treatment deal with the infection primarily. Two alternative procedures are available.

(1) **Sulphonamide Therapy.**—Employed locally the sulphonamides are useless in ophthalmia neonatorum, as they are inactivated by pus and break-down products of the tissues. Given by mouth they are highly effective. Originally small doses of the various sulphonamides were used, beginning with as low as one eighth of a $\frac{1}{2}$ -gramme tablet. Subsequently the initial dose was increased to 0.25 g. An initial dose of 0.5 g. of sulphamezathine has been used only recently. Tables I and II give the results in the earlier series and Table III comparative data for the second with the third series.

With sulphonamide treatment swelling of the lids generally subsides within twelve hours after admission; purulent discharge disappears within twenty-four hours, so that a threatening purulent ophthalmia becomes a simple conjunctivitis giving no anxiety.

TABLE I
EXPERIMENTAL SERIES OF 273 CASES TREATED WITH SULPHAPYRIDINE
(Initial dose up to 0.25 g.)

| Clinical Cure (days) | Local Treatment (classical methods) | | | General Sulphapyridine Treatment | | |
|-------------------------|-------------------------------------|----------|------------|----------------------------------|----------|-------------|
| | Gonococci | | Total | Gonococci | | Total |
| | Positive | Negative | | Positive | Negative | |
| Within 8 | 2 | 5 | 7 (15.2%) | 43 | 126 | 169 (61.9%) |
| 8-30 | 6 | 21 | 27 (58.7%) | 21 | 67 | 88 (32.2%) |
| More than 30 .. | 7 | 5 | 12 (26.1%) | 9 | 7 | 16* (5.9%) |
| Total | 15 | 31 | 46 | 73 | 200 | 273 |

*Including relapses after an apparent clinical cure.

TABLE II
COMPARATIVE RESULTS WITH SULPHONAMIDES IN 333 CASES OF OPHTHALMIA NEONATORUM
TREATED WITH A STANDARD DOSE
(0.25 g. on admission and 0.125 g. 4-hourly day and night until 48 hours after clinical cure)

| Clinical Cure | | | 1-3 days | | 4-8 days | | 9-30 days, relapses, poor response, and intolerance | | Total |
|--------------------|-----------|----------|----------|------|----------|------|---|------|-------|
| | | | No. | % | No. | % | No. | % | |
| Sulphapyridine .. | Gonococci | positive | 16 | 45.7 | 13 | 37.1 | 6 | 17.1 | 35 |
| | " | negative | 26 | 21.5 | 74 | 61.1 | 21 | 17.4 | 121 |
| | Total | | 42 | 27.0 | 87 | 55.7 | 27 | 17.3 | 156 |
| Sulphanilamide .. | Gonococci | positive | 1 | — | — | — | — | — | 1 |
| | " | negative | 6 | — | 3 | — | 4 | — | 13 |
| | Total | | 7 | 50.0 | 3 | 21.4 | 4 | 28.6 | 14 |
| Sulphamezathine .. | Gonococci | positive | 6 | 46.2 | 4 | 30.7 | 3 | 23.1 | 13 |
| | " | negative | 27 | 38.0 | 33 | 46.5 | 11 | 15.5 | 71 |
| | Total | | 33 | 39.3 | 37 | 44.0 | 14 | 16.7 | 84 |
| Sulphathiazole .. | Gonococci | positive | 7 | 63.6 | 4 | 36.3 | — | — | 11 |
| | " | negative | 8 | 22.2 | 24 | 66.6 | 4 | 11.1 | 36 |
| | Total | | 15 | 31.9 | 28 | 59.6 | 4 | 8.5 | 47 |
| Sulphadiazine .. | Gonococci | positive | 5 | — | 4 | — | — | — | 9 |
| | " | negative | 6 | — | 12 | — | 5 | — | 23 |
| | Total | | 11 | 34.4 | 16 | 50.0 | 5 | 15.6 | 32 |

TABLE III
RESULTS IN RELATION TO DOSAGE IN THE TREATMENT OF OPHTHALMIA NEONATORUM BY
SULPHONAMIDES ORALLY*

| Dosage | Number of cases | Percentage of cases showing | |
|---|-----------------|-----------------------------|--------------------------|
| | | Clinical cure in 1-3 days | Poor response or relapse |
| 0.25 g. initially, and 0.12 g. 4-hourly | | | |
| Different sulphonamides (sulphapyridine, sulphamezathine, sulphadiazine, sulphathiazole, and sulphanilamide) .. | 333 | 32.4 | 16.3 |
| Sulphamezathine only (included in the above series) .. | 84 | 39.3 | 16.7 |
| 0.5 g. initially, and 0.25 g. 6-hourly | | | |
| Sulphamezathine | 57 | 68.4 | 17.6 |
| Sulphamerazine | 24 | 87.5 | 0.0 |

* Data shown in Table II contrasted with results obtained in a small series treated with an initial dose of 0.5 g.

The eyes are either dry or very nearly so within twenty-four hours and in some two-thirds of all cases there is clinical cure within 72 hours.

The dreaded corneal complications of ophthalmia neonatorum do not develop. Such cases as are resistant to treatment are only relative failures with a somewhat prolonged course, which, however, does not give rise to anxiety, as there is conjunctivitis rather than purulent ophthalmia.

Babies tolerate oral sulphonamide well. Nothing is to be gained by using doses smaller than those indicated, and it is important to continue the

sulphonamides for 48 hours after clinical cure, as the too early suspension of treatment may lead to a relapse.

(2) Penicillin Treatment

(a) *Local Application of Drops.*—Unlike the sulphonamides penicillin remains effective in the presence of pus. It can, therefore, be used as a local agent, and has one other advantage over the sulphonamides in that cure is even more rapid. Treatment is rather exacting, and it is not as yet as standardized as oral sulphonamide therapy. In the use of

penicillin, concentration and frequency are all important.

Concentration.—Though some cases of ophthalmia neonatorum clear up readily on the instillation of penicillin drops, 500 units per ml. at hourly intervals, more fail to respond. Better results were obtained with a concentration of 1,000 units, and better still with one of 1,500 units per ml. There were only occasional failures when a concentration of 2,500 units per ml. was employed. These failures were largely confined to cases with inclusion bodies. If drops in a concentration of 10,000 units per ml. are used these resistant cases become fewer. Only white crystalline penicillin should be used, and the solvent should be only water of a low hypertonicity. As drops in such a concentration are well tolerated, nothing is gained by using lower strengths. A concentration of 10,000 units per ml. must therefore be regarded as the standard preparation.

Frequency.—With increasing frequency of application the course of the affection is cut down considerably. Distinctly better results are obtained when drops are put in at half-hourly instead of hourly intervals, whilst results are better still when the instillations are made every five minutes. With penicillin in a concentration of 2,500 units per ml. instilled at intervals of five minutes, all pus is suppressed within a matter of a few hours, and occasionally even within an hour. But even intervals of five minutes are too long, for penicillin drops are rapidly

washed out from the conjunctival sac. Instilled at intervals of one minute all tendency to pus formation is generally suppressed within half an hour, though the swelling of the lids will persist for several hours.

The use of ointments and lamellae has proved disappointing.

(b) Systemic Penicillin.—An experimental series of penicillin given by mouth proved disappointing. Results with penicillin given intramuscularly in doses of 200,000 units at three-hourly intervals were of the same order as with drops applied locally. Generally no treatment was necessary after 24 hours. The combination of oral administration and intramuscular injection did not prove particularly satisfying.

Table IV shows some of the more significant findings with the use of penicillin in the form of drops, and intramuscular injections, set out against causative organisms.

(3) Combined Sulphonamide and Penicillin Therapy.—In an attempt to reduce the frequency of poor responses, local penicillin therapy was combined with systemic sulphonamide therapy in a relatively small number of cases. The results do not appear to be superior to those obtained by one method only.

(4) Routine Procedures.—For the present there are two alternative methods of treating ophthalmia

TABLE IV
SUMMARY TABLE SHOWING RESULTS OBTAINED WITH PENICILLIN LOCALLY, AND PENICILLIN SYSTEMICALLY IN RELATION TO CAUSAL ORGANISM

| Organism | Drops at 5-minute intervals (2,500 U./ml.) | | Drops at 1-minute intervals | | | | Intramuscular injections 800,000 units in 4 doses of 200,000 U./ml. at 3-hourly intervals | | Total | |
|--|---|----|-----------------------------|----|-----------------|---|--|---|-------|----|
| | | | (2,500 U./ml.) | | (10,000 U./ml.) | | | | | |
| | + | — | + | — | + | — | + | — | + | — |
| Gonococcus | 7 | 3 | 7 | 2 | 6 | — | 4 | — | 24 | 5 |
| <i>Staph. aureus</i> | 12 | 4 | 12 | — | 2 | — | 1 | — | 27 | 4 |
| <i>Staph. albus</i> | 1 | — | 7 | 2 | 3 | 1 | 1 | 1 | 12 | 4 |
| Diphtheroids | 1 | 4 | 13 | 4 | 3 | 2 | 4 | 1 | 21 | 11 |
| <i>Str. haemolyticus</i> | 1 | — | 1 | — | — | — | — | — | 2 | — |
| <i>Str. viridans</i> | 1 | — | — | — | — | — | 2 | — | 3 | — |
| Pneumococcus | — | — | — | — | — | 1 | — | — | — | 1 |
| Gram-negative diplococci .. | — | 1 | — | — | — | — | — | — | — | 1 |
| Friedländer | 1 | — | — | — | — | — | 1 | — | 2 | — |
| Koch-Weeks | — | — | 3 | — | — | — | 1 | 1 | 4 | 1 |
| Morax-Axenfeld | 3 | — | — | — | — | — | — | — | 3 | — |
| No organisms | 1 | — | 3 | 1 | — | — | 5 | — | 9 | 1 |
| Virus presumed from presence of inclusion bodies | 12 | 3 | 7 | 9 | 11 | 4 | 14 | 3 | 44 | 19 |
| Total | 40 | 15 | 53 | 18 | 25 | 8 | 33 | 6 | 151 | 47 |

+ = Successful treatment.

— = Unsatisfactory response or relapse necessitating sulphonamide or further penicillin treatment.

neonatorum: sulphonamides orally and penicillin locally. Only rarely is it necessary to combine the two. The routine procedure for treatment in these cases may be thus summarized:

(a) *Steps in Common for the Two Methods.*—On admission a swab is taken for smear and culture and the eye is irrigated with half-normal saline at room temperature. A drop of adrenaline 1 in 1,000 is instilled and a scraping is taken from the palpebral conjunctiva for examination for the presence of inclusion bodies. Gutt. atropinae sulphas, 1 per cent., are instilled if the cornea is affected. Any pus that may have accumulated is wiped away with moist pledgets of cotton-wool.

(b) *Procedure for Sulphonamide Treatment.*

- (1) After the preliminary measures a tablet of sulphamerazine or sulphamezathine (0.5 g.) crushed into powder is given by mouth in a teaspoonful of water or milk. Alternatively a stock mixture can be used.
- (2) Sulphamerazine administration in doses of 0.25 g. is continued every eight hours. If sulphamezathine is used the administration has to be at six-hourly intervals.
- (3) Local treatment consists of three-hourly irrigation with saline solution during the first day in cases with profuse discharge; as a rule there is no need for further irrigation on the subsequent days. After irrigation medicinal paraffin is instilled as a precaution against the sticking together of the lids.
- (4) Atropine is instilled three times daily with corneal haze or ulceration.
- (5) Sulphonamide administration is continued for 48 hours after clinical cure.

With this treatment swelling of the lids generally subsides within 12 hours after admission; purulent discharge disappears within 24 hours.

(c) *Procedure with Local Penicillin Therapy.*

- (1) The preliminary measures are completed by the instillation of a drop of penicillin in a concentration of 10,000 units per ml. into the conjunctival sac.
- (2) The baby is now placed on the nurse's lap, while another nurse sitting near by instils one drop of penicillin solution, 10,000 units per ml., every minute for 30 minutes. Irrigation is not needed, as pus does not form to any extent; such thin mucoid discharge as is present can be ignored or, if it clings to the lid margin, wiped away with moist pledgets of cotton-wool.
- (3) At the end of this time there is invariably no pus and generally little or no discharge. The eye, however, is still moist, the lids are still swollen,

and the lid margins tend to be sticky. The baby is returned to its cot, and instillation of penicillin drops is continued six times at five-minute intervals, followed by a similar number of instillations at half-hourly, hourly, and two-hourly intervals. This gives a total of 22 hours' treatment. Many cases require no further attention.

- (4) In some babies the lid margins still tend to remain sticky. It is advisable in such cases to continue with penicillin at two-hourly intervals until the eye is dry, when treatment is carried on for a further 12 hours.

Crystalline penicillin only should be used for making up the drops. Impure penicillin is likely to cause irritative reactions.

The Prevention of Ophthalmia Neonatorum

The Credé procedure, compulsory notification, and modern methods of treatment have diminished the significance of ophthalmia neonatorum. With modern methods of treatment blindness from ophthalmia neonatorum need not occur, but no treatment will prevent blindness unless affected infants are treated early and adequately. The Public Health machinery in the control of ophthalmia neonatorum therefore remains pivotal. These measures have gone far in eliminating the complications of ophthalmia neonatorum, but have still left the incidence of the affection largely unaffected. Attention must now be focused on the prevention of ophthalmia neonatorum itself. The mechanical part of the Credé procedure—cleansing the lids—is invaluable; the value of its chemical component—the application of silver nitrate or its substitutes—must still be regarded as unproven. It is not in the search for better and more fool-proof antiseptics than silver nitrate that the hope of eliminating ophthalmia neonatorum lies. Rather is it in an intensive study of the various maternal infections that may lead to the affection, and the creation of Public Health machinery for the adequate antenatal treatment of such maternal infections. The experience gained in combating the ravages of ophthalmia neonatorum should be invaluable in the task of eliminating the disease altogether.

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